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# CHANGE IN RESPIRATION OF RAT LIVER MITOCHONDRIA DURING PROLONGED HYPOKINESIS

L. N. Grinberg

Translation of: "Izmeneniye dykhaniya mitokhondriy pecheni krys pri dlitel'noy gipokinezii," Voprosy Meditsinkoy Khimii, Moscow, Volume 16, 1970, pp. 387-90



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16. Abstract

Limitation of movement of periods of 10 and 20 days did not cause changes in the respiratory activity of rat liver mitochondria. Hypokinesis for a period of 30 days lead to an increase in mitochondrial respiration in the fourth state (against a background of succinate and α-ketoglutarate), into a decrease in the rate of respiration in the third state (against a background of α-ketoglutarate). A decrease in the magnitude of respiratory control was detected in the mitochondria under the influence of a 30-day long period of hypokinesis which was partially compensated for by the 60th day of the experiment. The magnitude of respiratory control after Chance-Williams was the most sensitive parameter which permitted estimates of change in the respiratory chain of mitochondria under the influence of hypokinesis.


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# CHANGE IN RESPIRATION OF RAT LIVER MITOCHONDRIA DURING PROLONGED HYPOKINESIS

L. N. Grinberg

Long term limitation of motor activity (hypokinesis) can cause functional disorders [1] and disorders with respect to the internal organs [2]. Changes in metabolism during hypokinesis are reflected in disorders of the water-salt equilibrium, a decrease in the rate of protein synthesis [3]; one observes dystrophic phenomena in the skeletal musculature as well [4]. In addition to this, increased activity of certain enzymes in the heart and liver tissue is noted [5, 6]. /387*

In the available literature we did not find data pertinent to the effect of hypokinesis on processes occurring in the mitochondria. In our study mitochondrial respiration was investigated; the mitochondria involved in the investigation were isolated from the livers of rats which were subjected to long term limitation of the capacity for free movement.

## The Method

Sixty-eight mongrel rats were used in the experiment. The subject animals were placed in individual cells 20 X 5 X 7 cm in dimensions which limited their capacity for movement in all directions. The animals of the control group were kept in common cages (4 to 5 rats per cage). The rats' weight at the beginning of the experiment was 160-190 g.

The mitochondria were isolated using a widely used method [7]. Absorption of oxygen was investigated in a closed cell by the aid of a platinum electrode. The PA-3 polarograph or the N-373 recorder were used for recording values.

The characteristic of metabolic conditions of the mitochondria used in the study corresponds to that accepted in the literature. The condition of intensive respiration of mitochondria accompanied by phosphorylation of ADP added from without is the third (or active) state (Figure 1). When the exogenic

*Numbers in the margin indicate pagination in the foreign text.

ADP is exhausted, consumption of oxygen by the mitochondria spontaneously flows and reaches the fourth (or controlled) state. Transition from the third state to the fourth state reflects the degree of energetic regulation of respiration in the mitochondria which is expressed quantitatively by the magnitude of respiratory (acceptor) control after Chance-Williams.

## Results and Discussion

Measurement of the respiratory activity of rat liver mitochondria in the early periods of hypokinesis (10 and 20 days) did not reveal differences between the subject and control animals. Change in the rate of respiration of mitochondria occurred under the influence of hypokinesis lasting 30 days. In Figure 1, samples of the obtained curve and diagram representing the rate of oxygen consumption (in micromoles per one second) by mitochondria against a background of substrate without ADP, after adding ADP, and during transition to the fourth state are given.

Most significant is the fact that with 30-day long hypokinesis (curve b), the weight of mitochondrial respiration in the fourth state exceeds by more than 3 times this value in the control (curve a) with the use of succinate. Here the intensity of oxygen absorption in the third (phosphorylating) state is the same in both curves.

In the case of the NAD-dependent substrate (α-ketoglutarate), respiration of mitochondria of the hypokinetic animals (curve d) is characterized by an increase in the rate of respiration in the fourth state and a decreased rate in /388
third state, in comparison with the control (curve c).

The capacity of the mitochondria to hasten the transport of electrons along the respiratory chain when ADP is added, and also for transition to the fourth (regulated) state (see Figure 1) is quantitatively expressed by the magnitude of respiratory control after Lardy-Wellman and after Chance-Williams, respectively. Inasmuch as a 30-day long period of hypokinesis led to a change in the relationship between the rate of mitochondrial respirations, one could expect that this will be reflected as well in the value of respiratory control. Actually, significant fluctuations in the values of respiratory control were found under the influence of a multiday long period of hypokinesis.

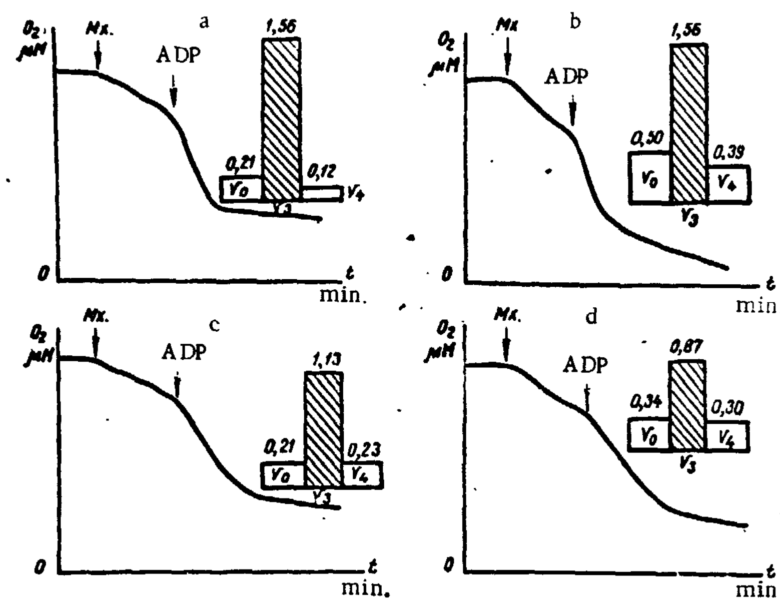


Figure 1. The Effect of a 30-Day Long Period of Hypokinesis on the Rate of Mitochondrial Respiration. The incubation medium containing KCl (15 mmol), $MgCl_2$ (10 mmol), $KH_2PO_4$ (15 mmol), saccharose (0.2 mmol), succinate (10 mmol) or α-ketoglutarate (10 mmol); pH medium 7.50. Arrows show moments of adding mitochondria (amount of mitochondria from 250 mg moist tissue per sample) and ADP (200 mkmol). a, Control (substrate of respiration — succinate); b, hypokinesis, 30-day period (succinate); c, control (α-ketoglutarate); d, 30-day long period of hypokinesis (α-ketoglutarate).
Note: Commas indicate decimal points.

Change in the degree of intensity of respiration and phosphorylation characterized by the magnitude of respiratory control, in the mitochondria of rat livers during long term hypokinesis is shown in Figure 2, from which one can see that a decrease in the magnitude of respiratory control is particularly pronounced at the 30th day of hypokinesis, while by the 60th day one detects a tendency toward an increase in its value.

It is important to note that the sharpest fluctuations were those in the value of respiratory control after Chance-Williams during oxidation of succinate by the mitochondria (shaded diagram in the right half of Figure 2). In connection with this, the magnitude of respiratory control after

Chance-Williams can serve as a sensitive criterion for estimating changes in the respiratory chain of mitochondria during hypokinesis.

As is known, the value of respiratory control reflects the degree of intensity of electron transport along the respiratory chain of the mitochondria with the process of accumulation of energy in the ATP molecule during this process. However the energy of biological oxidation, being locked in the macroergic precursors of ATP can, under certain conditions, fail to convert into a /389
form of phosphate bond, and can be expended on providing active transport of ions, structural changes, and also on the reduction of NAD by means of shifting a flux of electrons into the respiratory chain [8]. In such a case there is an increase in the intramitochondrial expenditure of energy-rich compounds and one notes a diminution of the regulatory effect of exogenic ADP (a decrease in the magnitude of respiratory control).

In the literature, facts of the physiological role of processes in the mitochondria occurring at a low degree of intensity have accumulated. It has been shown that electron transport and energy conversion in such mitochondria lead to increased heat production and also supports the active transport of ions, processes of detoxication, oxidation and liberation [9, 10]. In this case one can record an extremely low magnitude of respiratory control during exposure to exogenic ADP.

The decrease in the magnitude of respiratory control after Chance-Williams which was observed in our experiments with a 30-day long period of hypokinesis was caused predominantly by an increase in the rate of mitochondrial respiration in the regulated state.

As has been said, during hypokinesis one notes a predominance of catabolic reactions and elimination from the organism of significant amounts of water, cations, nitrogen, and other metabolic products [3]. One could think that the increase in mitochondrial oxygen absorption observed by us during hypokinesis, with a certain decrease in the phosphorylating activity of the mitochondria is linked with activation of processes of metabolite oxidation and an increase in the transport of ions in the cell. The latter fact deserves particular attention in view of the fact that calcium, for example, is capable of reacting with the macroergic precursor of ATP and thereby of decreasing the effectiveness of phosphorylation [1].

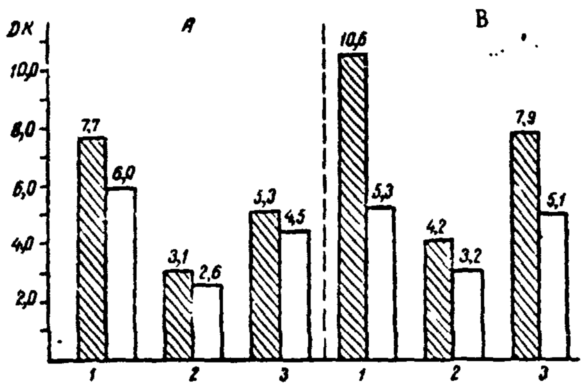


Figure 2. Change in Respiratory Control in the Rat Liver Mitochondria Dependent Upon the Duration of Hypokinesis. A, Respiratory control after Lardy-Wellman; B, respiratory control after Chance--Williams. Shaded columns, succinate; white columns, ketoglutarate; 1, control, 2, 30-day long hypokinesis; 3, 60-day long hypokinesis.
Note: Commas indicate decimal points.

In conclusion it is necessary to note that succinate has the capacity to monopolize the respiratory chain and to provide an extremely high rate of electron transport in the formation of energy-rich compounds [3]. It is possible that during hypokinesis the role of succinate as an oxidizing substrate increases, which is indicated by the extremely significant increase in mitochondrial respiration in the fourth state and by the absence of a decrease in the rate of respiration in the third state under the influence of hypokinesis (against a background of succinate but not against a background of α-ketoglutarate).

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[1] Translator's Note: The author of item 2 and the first author of item 6 are presented inaccurately here due to poor copy quality of the foreign text.

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